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Reviewed by: Byron T. Backus Byron T. Backus 3/31/89
Section 2, HFASB (H7509C)

Secondary Reviewer: K. Clark Swentzel K. Clark Swentzel 4/3/89
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DATA EVALUATION REPORT I

STUDY TYPE: Acute Oral Toxicity in Rats TOX CHEM NO. 309BB

MRID NO: ACC. NO: 408064-2

TEST MATERIAL: TD 2073 (97.0%)

SYNONYMS: Potassium 3,4-dichloro-5-isothiazole carboxylate
AC 303,358 Chemical Hybridizing Agent; CHEMBRED

STUDY NUMBER(S): WIL-75019

SPONSOR: Pennwalt Corporation
Agrichemical Division
P.O. Box 1027
Puyallup, Washington 98371

TESTING FACILITY: Wil Research Laboratories, Inc.
Ashland, Ohio 44805-9281

TITLE OF REPORT: Acute Oral Toxicity (LD50) Study in Albino Rats with TD 2073

AUTHOR(S): Naas, D. J., Bates, D. C., Nemec, M. D., Laveglia, J.

REPORT ISSUED: 1/10/86

CLASSIFICATION: Core supplementary data (female oral LD_{50} inadequately defined)

CONCLUSIONS:

1. The study adequately defines a rat acute oral LD_{50} of 956 (839-1088) mg/kg for males; however, the female oral LD_{50} (reported as less than 683 mg/kg) is insufficiently defined. Additional data should be obtained to more adequately establish the female oral LD_{50} value for this test material.

A. MATERIALS:

1. Test compound: TD 2073, 97.0%, lot no. N.B. 86-58-1. Described as an off-white powder. The test material was ground into a fine powder and suspended in Mazola^{R} corn oil for purposes of dosing.

2. Animals used: Young Sprague-Dawley COBS^{R} CD^{R} rats from Charles River Breeding Laboratories, Inc., Portage, Michigan. "The animals weighed from 225 to 298 grams at study initiation."

B. STUDY DESIGN:

1. Test material administration:

The test material was orally administered (by gastric intubation) at dosage levels of 683, 826 and 1000 mg/kg suspended in corn oil at a constant volume of 10 ml/kg to groups of 5M and 5F rats which had been fasted for 18 hours prior to dosage.

2. Quality assurance:

There is a signed and dated Good Laboratory Practices Compliance Statement on p. 3 of the report, which states: "The submitter of this study was neither the sponsor of this study nor conducted it, and does not know whether it has been conducted in accordance with 40 CFR Part 160." There is a laboratory Quality Assurance Unit Statement on p. 17.

C. METHODS AND RESULTS:

1. Observations:

"The animals were observed for treatment-related effects on the day of dosing and for a subsequent fourteen day observation period. Mortality, clinical observations, body weights and gross necropsy findings were recorded."

Results:

The following mortality was observed:

Dosage Level (mg/kg)	Mortalities/Rats dosed M	F
683	0/5	3/5
826	1/5	3/5
1000	3/5	5/5

All deaths occurred within the first 24 hours after dosage.

The male LD_{50} was calculated as 956 mg/kg with 95% confidence limits of 839-1088 mg/kg. The female LD_{50} was calculated as less than 683 mg/kg (no 95% C.L. could be obtained from the data). The combined LD_{50} was 825 (716-951) mg/kg.

Symptoms:

Reported as lethargy, loss of voluntary muscle control (primarily ataxia, but also impaired righting reflex and prostration). "All females and more than one-half the males also exhibited body tetany (rigidity) that was induced by touch. More than one-half of all rats on study had urogenital staining. Diarrhea was also noted for more than one-half of the rats, although this may be related to the vehicle used (corn oil)." Other findings included staining around the mouth, hypersensitivity to touch, salivation, bradypnea, high carriage, ocular discharge, respiratory rales, decreased urination, decreased defecation, dried red material around the mouth and red material on cage paper. Most symptoms were observed in the period from day 0 to day 2. "Essentially all rats that survived to study termination appeared normal by day 6."

2. Body weights:

One male in 826 mg/kg group is reported as having lost 13.0 grams in the period from day 7 to day 14. Otherwise, survivors generally gained weight.

3. Necropsies:

"Gross necropsy examinations of the major organ systems of the thoracic and visceral cavities were performed on all rats that died or were sacrificed at study termination. Sacrifice was by carbon dioxide asphyxiation."

Results:

From the summary, p. 14: "Changes were noted in the kidneys (dark red or cortico-medullary junction reddened), lungs (bright to dark red) and brain (hemorrhagic and dilated meningeal vessels) for essentially all rats that died. In addition, gastrointestinal abnormalities (loss of epithelium and/or reddened mucosa) and thymus glands that were dark or had dark red areas, were noted for more than one-half of the rats that died."

"Enlarged adrenals were present for approximately one-half of the female rats that died...(but) was not noted among male rats that died."

"There were no significant changes observed for all tissues examined for rats that were terminally sacrificed."

D. DISCUSSION:

The study adequately demonstrates that the acute oral LD_{50} for male rats is 956 (839-1088) mg/kg. However, the female acute oral LD_{50} (reported as <683 mg/kg) is insufficiently defined. Additional data should be obtained to more adequately establish the female oral LD_{50} value for this test material.